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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/759,731	01/16/2004	Christopher J. Bond	11669.136USU1	6901

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EXAMINER	
GROSS, CHRISTOPHER M	

ART UNIT	PAPER NUMBER
1639	

MAIL DATE	DELIVERY MODE
08/20/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/759,731	BOND, CHRISTOPHER J.	
	Examiner	Art Unit	
	CHRISTOPHER M. GROSS	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *See Continuation Sheet* is/are pending in the application.

4a) Of the above claim(s) *See Continuation Sheet* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *105-107,109-111 and 113-128* is/are rejected.

7)☒ Claim(s) *122* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/30/2008;7/3/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims pending in the application are 1-7,9-12,15,16,18-24,29-34,36-40,42,44-46,48-54,59-66,68-74,76,81-85,90-96,98,99 and 105-130.
Continuation of Disposition of Claims: Claims withdrawn from consideration are 1-7,9-12,15,16,18-24,29-34,36-40,42,44-46,48-54,59-66,68-74,76,81-85,90-96,98,99,108,112,129 and 130.

DETAILED ACTION

Responsive to communications entered 5/3/2008. Claims 1-7,9-12,15,16,18-24,29-34,36-40,42,44-46,48-54,59-66,68-74,76,81-85,90-96,98,99, 105-130 are pending. Claims 1-7,9-12,15,16,18-24,29-34,36-40,42,44-46,48-54,59-66,68-74,76,81-85,90-96,98,99,108,112, 129,130 stand withdrawn. Claims 105-107,109-111,113-128 are examined herein.

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 5/30/2008 has been entered.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Priority

Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application); the disclosure of the invention in the prior application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See Transco Prods., Inc. v. Performance Contracting, Inc., 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994) [taken from MPEP 201.01]

The instant application, filed 1/16/2004 claims priority to provisional application 60/441,059 filed 01/16/2003 (referred to as '059) and claims benefit of provisional application 60/488,610 (referred to as '610) filed 07/18/2003 and claims benefit of provisional application 60/510,314 filed 10/08/2003.

Nevertheless, support for a CDRH3-phage coat fusion protein comprising a "N terminal portion of about 1 to 4 amino acids in which some or all amino acid positions are structural" and a "C terminal portion of about 1 to 6 amino acids in which some or all amino acid positions are structural" as set forth in amended claim 105 is not disclosed in the earlier applications.

It is further noted that support for a fusion protein comprising at least a portion of a phage coat protein is not supported in the earlier applications in that at least a portion reads on as little as one amino acid residue.

See also 35 USC 112 first paragraph considerations concerning new matter below.

Therefore 1/16/2004 remains the date for the purposes of prior art concerning claims 105-107, 109-111,113-128.

Response to Arguments

Applicant argues that support for the subgenera "N terminal portion of about 1 to 4 amino acids in which some or all amino acid positions are structural" and a "C terminal portion of about 1 to 6 amino acids in which some or all amino acid positions are structural" is found on **p 18 of '059 or p 18 of '610 or p 113 of '610, see first quotation on p 21, first quotation on p 23 and the quotation bridging pp 23-24 of**

remarks entered 5/30/2008. While said quotations provide support for the *last* six residues of the CDHR3 domain being structural they do not provide support for the considerably broader "a C terminal portion of about 1 to 6 amino acids," set forth in claim 105, such that a C terminal *portion* may be construed as located anywhere following the protein N terminus. Furthermore fusion proteins are not mentioned in said quotations on p 18 of '059 or p 18 of '610 or p 113 of '610.

Applicant argues that support for the subgenera "N terminal portion of about 1 to 4 amino acids in which some or all amino acid positions are structural" and a "C terminal portion of about 1 to 6 amino acids in which some or all amino acid positions are structural" is found on **p 21 of '059 or p 22 of '610, see quotation bridging pp 21-22 of remarks entered 5/30/2008 and second quotation on p 23 of remarks entered 5/30/2008**. While said quotations provide support for the *first* four residues of the CDHR3 domain being structural, they do not provide support for the considerably broader "an N terminal portion of about 1 to 4 amino acids," set forth in claim 105, such that a N terminal *portion* may be construed as located anywhere before the protein C terminus. Furthermore fusion proteins are not mentioned in said quotations on p 21 of '059 or p 22 of '610.

Applicant argues that support for the subgenera "N terminal portion of about 1 to 4 amino acids in which some or all amino acid positions are structural" and a "C terminal portion of about 1 to 6 amino acids in which some or all amino acid positions are structural" is found on **p 58 of '059, see first quotation on p 22 of remarks entered 5/30/2008**. Here it is noted that said quotation provides support for 1-20, 5-15 or 10-20

insertions with no mention regarding N or C locations, as set forth in claim 105. Furthermore fusion proteins are not mentioned in said quotation on p 58 of '059.

Applicant argues, that support for the subgenera "N terminal portion of about 1 to 4 amino acids in which some or all amino acid positions are structural" and a "C terminal portion of about 1 to 6 amino acids in which some or all amino acid positions are structural" is found on **p 99 of '059**, **see second quotation on p 22 of remarks entered 5/30/2008.** Here it is noted that said quotation provides some support for fusion proteins, but no mention is made of N and C terminal structural amino acids. Also noted is that p 99 of '059 recites the method used to prepare the pIII fusion proteins employed the vector pS1602 reported by Sidhu et al (2000 J. Mol. Biol. 296:487-495 and Lowman et al 1991 Biochemistry 30:10832– IDS entries 9/27/2004). With pS1602, sequences of interest, such as human growth hormone, CDHR domains, etc are fused to the N terminus of pIII according to Sidhu et al who cites Lowman et al on p 652 left column line 6, in contrast claim 105 is comprise *any* phage coat protein fused at either terminus of coat protein.

Applicant argues, that support for the subgenera "N terminal portion of about 1 to 4 amino acids in which some or all amino acid positions are structural" and a "C terminal portion of about 1 to 6 amino acids in which some or all amino acid positions are structural" is found on **p 107 of '059, see third quotation on p 22 of remarks entered 5/30/2008.** Here it is noted that said quotation refers to a RLR...WFVV consensus sequence which does not provide support for the complete *range* of 1 to 4 N structural terminal amino acids (e.g. 3 structural residues at positions 2,3 and 4) per "N terminal

portion of about 1 to 4 amino acids in which some or all amino acid positions are structural" set forth in claim 105. Similarly, said consensus sequence does not provide support for complete *range* of 1 to 6 C structural terminal amino acids (e.g. structural residues at positions n-6 ,n-5 and n, where n is the ultimate or last residue of the CDHR3 domain) per "C terminal portion of about 1 to 6 amino acids in which some or all amino acid positions are structural" as set forth in claim 105 Furthermore, said consensus sequence does not provide support "a C terminal portion of about 1 to 6 amino acids," set forth in claim 105, in that a C terminal portion may be construed as located anywhere following the protein N terminus. Even further, said consensus sequence does not provide support for "an N terminal portion of about 1 to 4 amino acids," set forth in claim 105, in that a N terminal *portion* may be construed as located anywhere before the protein C terminus. Finally, fusion proteins are not mentioned in said quotation on p 107 of '059.

Applicant argues, that support for the subgenera "N terminal portion of about 1 to 4 amino acids in which some or all amino acid positions are structural" and a "C terminal portion of about 1 to 6 amino acids in which some or all amino acid positions are structural" is found in figures **45 and 46 of '059 and figure 45 of '610, see paragraph bridging pp 22-23 and first full paragraph p 24 of remarks entered 5/30/2008.** Here it is noted that figures set forth in the provisional applications appear to list the individual species used to generate the consensus sequence mentioned above, and similarly in this regard said species do not provide support for the same reasons as said consensus sequence. Again, fusion proteins are not shown in the figures of '059 and '610.

In summary, the sections pointed to by applicant do not provide adequate support for the claimed subject matter and consequently 1/16/2004 is the date for the purposes of prior art concerning claims 105-107, 109-111,113-128.

Withdrawn Rejection(s)

The rejection of claims 123-126,127 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is hereby withdrawn in view of applicant's amendments to the claims.

Maintained Claim Rejection(s) - 35 USC § 102

Claims 105-107, 109,111,113,115-128 are rejected under 35 U.S.C. 102(a) as being anticipated by **Bond et al** (2003 J. Mol. Biol. 332:643-655 – IDS entry 9/27/2004).

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 105-107, 109,111,113-128 are rejected under 35 U.S.C. 102(a) as being anticipated by **Bond et al** (2003 J. Mol. Biol. 332:643-655 – IDS entry 9/27/2004).

The claimed subject matter per claim 105 is drawn to a fusion protein comprising:

> at least a portion of a phage coat

protein fused to a binding polypeptide comprising a heavy chain variable domain comprising a CDRH3 scaffold comprising: an N-terminal portion of about 1 to 4 amino acids in which some or all amino acid positions are structural; a C terminal portion of about 1 to 6 amino acids in which some or all amino

acid positions are structural, and c)a central portion or loop of about 1 to 20 contiguous amino acids that can vary in sequence and in length.

Claims 106-107, 109,111,113-128 represent variations thereof.

Bond et al teach, through out the document and especially the abstract, structural contributions made by CDR3 loops in camelid V_HH domains.

Said CDR3 loops in camelid V_HH domains are taken as a CDRH3 scaffold, as set forth in claim 105 and defined in paragraph 0014 of the present published application (i.e. CDRH3 is the CDR3 of the heavy chain). Bond et al teach construction of a llama anti-human chorionic gonadotropin (alphaHCG) V_HH fused to phage coat protein P3 on p 652, first paragraph. Bond et al teach in the paragraph bridging pp 644-645, the anti-alphaHCG structure comprises Trp 100 packing against Phe 37 and the aliphatic portion of Arg 45. Said Phe 37 and Arg 45 are taken as two structural amino acid positioned in the N terminal portion of claim 105. Said Trp 100 is taken as one structural amino acid positioned in the C terminal portion of claim 105. Bond et al teach on p 645 last paragraph insertions into said anti-alphaHCG at the short seven residue CDR3 loop, therein accommodating insertion of a central portion, reading on claim 105.

Bond et al teach in figure 1, camelid V_HH domains may comprise a disulfide bond between residues Cys 33 and Cys 109, reading on claim 106.

Bond et al teach in the table in figure 4a, a V_HH bearing a 17 residue insert comprising the sequence RIGR-...-WVTW (elected species) as an insert, reading on: R-L/I/MA_3-R when A_3 is Gly, as set forth in claim 107; the R-I of claim 109; the W-V of claim 111; C terminal portion being 4 amino acids of claim 113; center portion being 9

amino acids of claim 114; R-L/I/MA_3-R when A_3 is Gly and W-A7-A8-A9-A10-A11, wherein A7-11 can be any amino acid as set forth in claim 115.

Bond et al teach on p 649 second paragraph and figure 3b, shotgun alanine scanning as indicative of RI and WV being structural in said RIGR...WVTW insert, as set forth in claim 116-120.

Said WV is in positions 100i and 100j, according to figure 4a of Bond et al, as set forth in claim 121. Said figure 4a of Bond et al includes species bearing a central portion having at least one variant amino acid encoded by a non-random codon set as set forth in claim 122.

Said Phe 37 reads on the phenylalanine of claim 124 and hydrophobic residue of claim 123. Said Arg 45 reads on the arginine of claims 125 and 123. Bond et al teach Threonine at position 91 in figure 2, which appears to be in another framework region, reading on claim 126.

Said RIGR-...WVTW insert of Bond et al in figure 4a is 17 residues and reads on claim 128 when A1 is R, A2 is I, A3 is G, A4 is R, n is 9, A6 is S, A7 is W, A8 is V, A9 is T and A10 is W.

Please note that the above rejection has been modified from the original version to more clearly address applicants' newly amended claims and/or arguments.

Response to Arguments

On p 24 of the remarks entered 5/30/2008, applicant argues that the claimed subject matter is entitled a priority date of at least 1/16/2003, thus Bond et al does not

constitute prior art. In light of the lack of support in the provisional applications, however, as discussed in the priority section above, 1/16/2004 is the date for the purposes of prior art concerning claims 105-107, 109,111,113-128 and accordingly Bond et al constitutes prior art under 35 USC 102(a).

Maintained Claim Rejection(s) – Double Patenting

Claims 105,107, 109,111,113,115-122,127-128 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 22, 25,26,30,31,35-37,48-50 of copending Application No. 11/102502 (referred to as '502) in view of **Sidhu et al** (2000 J. Mol. Biol. 296:487-495 – IDS entry 9/27/2004) and evidenced by Bond et al (2003 J. Mol. Biol. 332:643-655 – IDS entry 9/27/2004).

Response to Arguments

On p 27 of applicants remarks entered 5/30/2008, applicant requests that the provisional rejection be held in abeyance until allowable subject matter is indicated.

Applicants request have been considered, however the rejection will not be held in abeyance because the abeyance provision set forth in MPEP 804 applies to applications lacking rejections on other grounds and claim 105 at least of the present application stands rejected 35 USC 102 and 112 first paragraph. Therefore claims 105,107, 109,111,113,115-122,127-128 remain provisionally rejected on grounds of double patenting.

Maintained Claim Rejection(s) - 35 USC § 112

Claims 105-107, 109-111,113-128 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a "new matter" rejection.

Response to Arguments

Applicant has successfully pointed to support for CDRH3-phage coat fusion protein bearing a C terminal sequence CWVTW, as set forth in claim 110.

Applicant has successfully pointed to support for CDRH3-phage coat fusion proteins with structural limitations concerning a C terminal portion of about 1 to 6 amino acids in which some or all amino acid positions are structural on p 7 line 12 of the present specification.

On pp 25-26 of applicant's remarks entered 5/30/2008, applicant alleges (in the underlined passages) quoted from the present specification provide support for "an N-terminal portion of about 1 to 4 amino acids in which some or all amino acid positions are *structural*." The examiner respectfully disagrees in that none of the passages recited show support for the third residue being structural and accordingly this rejection is hereby maintained.

New Claim Rejection(s) – 35 USC § 112

The following is a quotation of the **first** paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 105-107, 109-111,113-128 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection concerns new matter.

Claim 1 is drawn to a fusion protein comprising *at least a portion* of a phage coat protein.

Claim 123 has been amended such that the residue at framework position 45 may be any hydrophobic amino acid.

Claim 126 has been amended to include another framework region.

The specification as originally filed provided no implicit or explicit support for a fusion protein comprising a portion of a phage coat protein, which reads on as little as one amino acid.

The specification as originally filed provided no implicit or explicit support for the residue at framework position 45 being Ile Val, etc. (i.e. hydrophobic amino acids).

The specification as originally filed provided no implicit or explicit support for two framework regions.

Applicants are reminded that it is their burden to show where the specification supports any amendments to the disclosure. See MPEP 714.02, paragraph 5, last sentence and also MPEP 2163.06 I.

MPEP 2163.06 notes "If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. *In re Rasmussen*, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)." MPEP 2163.02 teaches that "Whenever the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was filed...If a claim is amended to include subject matter, limitations, or terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in that application. MPEP 2163.06 further notes "When an amendment is filed in reply to an objection or rejection based on 35 U.S.C. 112, first paragraph, a study of the entire application is often necessary to determine whether or not "new matter" is involved. *Applicant should therefore specifically point out the support for any amendments made to the disclosure.*

New Claim Objections

Claim 122 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 105 is drawn to a

fusion protein comprising a phage coat protein fuses to a CDHR3 scaffold, whereas claim 122 is drawn to multiple fusion proteins bearing at least one variant amino acid in the center portion.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher M. Gross whose telephone number is (571)272-4446. The examiner can normally be reached on M-F 9-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, J. Douglas Schultz can be reached on 571 272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Christopher M Gross
Examiner
Art Unit 1639

cg

/JD Schultz, PhD/

Supervisory Patent Examiner, Art Unit 1635